required for the formation of fungus. It is in fact to defective ventilation and high hygrometric conditions of the atmosphere that the unhealthiness of Rio de Janeiro is attributed.

During the great epidemic of yellow fever of 1872 at Montevideo the disease showed an inexplicable predilection for attacking houses fronting to the north. Now the houses on the north side of streets in Montevideo are conspicuous for their dampness. It is, therefore, probable that the factor of humidity whether on board ships, along the coast or in the interior, is the principal coefficient in this biologic phenomenon, and not some commonplace meteorological influence. On the other hand the natural resistance of the icteroid bacillus to desiccation, nature's method of disinfection, and its longevity in sea water are sufficient to explain the acclimatization of icteroid typhus on ships and in maritime localities.

Extract from a paper entitled "Experimental and Anatomical Researches in Yellow Fever."

[Transmitted by Passed Assistant Surgeon H. D. GEDDINGS—Translated in this Bureau from the Annals de l'Institut Pasteur, Paris, June 25, 1897.]

By Dr. W. HAVELBURG, Rio de Janeiro.

The idea of looking for the specific germ of yellow fever in the contents of the stomach and intestines naturally suggests itself. Yellow fever begins with gastric symptoms. This condition of the stomach and intestines continues throughout the disease.

But this study of stomachic flora seemed to me so difficult that I endeavored to avoid it by making plantings from the organs most attacked, even from those which presented nothing from the anatomic point of view. The first plantings on gelatin of the substance of the liver, kidney, spleen, the mesenteric glands, the walls of the biliary vessels, the blood, and the bile remained sterile, especially in the first cases examined. It was only after continued experiment that I saw appear in the sporadic state, now in one organ, now in another, and always very much disseminated, colonies of a microbe, which I found also when I studied the contents of the stomach and intestines and the famous black vomit which gives to this disease its specific character. I found this microbe with a certain constancy in all cases, and in grave cases it was almost the only inhabitant of the blood contents of the stomach. Moreover, it showed itself pathogenic for the guinea pig.

This fact gave me the idea of isolating it by passage through this animal, and from the first this attempt was attended with good results.

Before describing them, I will allude to an important question suggested to me by Dr. Roux. In the absence of a microorganism in the organs and liquids, is it possible to find a toxic substance circulating in the body which may produce manifestations of the disease? After some fruitless attempts in several directions I drew blood, with a sterilized syringe, from a vein of the arm, prepared as for bleeding, and immediately injected this blood into the peritoneal cavity of a guinea pig. Former experiments showed me that these animals support relatively large quantities of human blood. Ten cubic centimeters of blood taken from a person who was seriously ill, and who died next day, produced in the animal slight malaise, which disappeared next day. A slight rise of temperature of 38.7° to 39.7° continued some days.

In five days the animal had lost 60 grams of its weight, but it subsequently recovered. I repeated this experiment with another patient, also seriously attacked, and with the same success. These facts do not speak in favor of the special efficacy of a toxic substance existing in yellow fever. It then occurred to me that to place a guinea pig, weighing 500 grams, in the same conditions, relatively, to the blood injected, I should inject about 35 grams of the blood of the patient. I repeated my experiments when the patient was dying and injected a guinea pig, weighing 535 grams, with 30 grams of blood. The initial temperature was 38.7°. It rose to 39.9° and remained at this point for two days. On the fourth day the temperature fell to 37.1°. and the animal died. This experiment was repeated with 4 patients severely attacked, the prognosis being doubtful in all the cases. The results in the case of the guinea pig solved the problem, not only as to the existence of a poison, but as to the intensity of the disease. All 4 animals became sick. Two of them are dead, as are also the persons whose blood they received. The two other patients will recover, also the guinea pigs injected. The existence of a toxic substance in yellow fever is, therefore, indubitable.

The most important experiment, with the point of departure for any other researches, is the following:

When we inject under the skin of a guinea pig 1 to 2 c. c. of the contents of the stomach of a person dead of yellow fever, the animal infallibly dies, and we find in his blood, in pure culture, the microorganism which I believe I may consider specific.

This fact was verified 21 times in the cases I examined in 1896. No case gave negative results. In 10 complete necropses the diagnosis of yellow fever was incontestable. In the other partial necropsies I made bacteriological examination of the contents of the stomach, and at the same time verified macroscopically and microscopically the alterations proper to the disease.

In two control experiments consisting of a hypodermic injection of the same quantity of the stomach contents of persons dead of another disease, the guinea pigs remained alive.

When yellow fever material is used the guinea pig dies after the injection, and the result is the same whether the contents of the stomach be sanguineous or catarrhobilious, which happened in two cases. Death supervened in from eight to twenty-four hours. In one case, which clinically was very grave, I saw a guinea pig, weighing about 400 grams, die five hours after a hypodermic injection of 1 c. c., and notwithstanding this short space of time the existence of bacilli in the blood of the heart was abundant. The simplest means of obtaining a pure culture of the pathogenic germ is by the hypodermic injection of guinea pigs.

This microorganism is a small and extremely slender bacillus, the length of which is about 1 micromillimeter and the width from 0.3 to 0.5 micromillimeter. It is a straight rod, generally isolated, but often occurring in pairs. It does not show flagellæ in any of the several culture media. The two poles of the bacillus are more brilliant, and this property, which recalls the bacillus of chicken cholera, makes it resemble a diplococus. In fresh and recent cultures, half of the microorganisms present this appearance, which is most frequent when the bacillus is most virulent. It colors easily with all the colors which have an aniline base, but suffers decoloration from absolute alcohol and acids. It does not take coloration by the Gram method; with weak solutions we may succeed in coloring it distinctly.

I at first thought the bacillus motile. I have not succeeded in coloring the flagellæ by the Lœffler method, as its movements persist in antiseptic solutions, and after three hours' exposure to a temperature of 65° the movement must be Brownian. I have seen no sign of spore formation.

On a gelatin plaque the bacillus grows visibly at the end of twenty-four hours like a white point, which increases in size during twenty-four or forty-eight hours. The gelatin is not liquefied. The colonies, whether large or small, exhibit a yellowish disk, finely granulated with a finely indented border.

Puncture of the gelatin makes the microorganism grow at a depth in the form of a fine thread, consisting of white grains. On the surface they form a thick, white cupola, shaped like a nail head.

On the surface of the gelose, it forms, when the planting is not very copious, round, grayish white disks, which may remain isolated or commingle. When it is planted in streaks on gelose, grayish white masses are seen to form, which, starting from the points planted, extend on all sides, but the growth is very limited.

Common broth clouds rapidly. After twenty-four hours we find a cloudy gray deposit, which soon condenses when agitated. The deposit is never very considerable. The surface of the bouillon remains clear. It is only in old cultures that a thin and slender layer is formed which precipitates when the liquid is agitated, leaving a layer more or less adherent on the walls of the glass. Cultures in bouillon always have a disagreeable odor and always retain an alkaline reaction.

Sugar bouillon ferments rapidly. In gelose which contains either sugar of milk or glucose the formation of gas is observed.

At the end of twelve hours the milk is coagulated. On potato, culture is relatively slight, and it is covered with a grayish layer.

In blood serum the microorganism does not grow in characteristic manner. The serum is troubled and forms a deposit. On coagulated serum a thin gray layer forms.

The production of indol is always very intense. There is also a considerable production of hydrosulphuric acid.

The microorganisms grow also in media of acid cultures, even when the acidity is very intense.

Gelose with litmus is not discolored, unless it contains sugar.

The microorganism is a facultative anærobe. In the absence of air and in hydrogen its culture is luxuriant, and it appears to have more virulence than is observed for other microorganisms.

The infection of the guinea pig is possible hypodermically and by the intraabdominal process. If 1 c. c. of a bouillon culture, hypodermically administered, is enough to kill the animal in twenty-four hours, 0.2 c. c. would produce this effect administered intraabdominally. Death may be caused more quickly with larger doses. Small doses prolong the duration of the disease and the animal becomes very thin. Some escape and recover.

Whatever be the progress of the disease, whether slow or rapid, whether the injection be made with the stomach contents or with the culture of my microorganisms, we always find this microorganism in pure culture in the blood of the heart of the animal.

The mouse has the same receptivity. About 0.1 c. c. of the bouillon culture injected into the peritoneal cavity is sufficient to cause death in six hours. After a hypodermic injection of 0.25 c. c. the animal dies in twenty-four hours.

It is somewhat different with rats. I have found some which did not react, with either hypodermic or intraabdominal injection. Most of them have a certain disposition to react to injection of the contents of the stomach, and also of my cultures.

The chicken has an almost perfect immunity. We may inject either the contents of the stomach or the culture subcutaneously, or into the abdominal cavity, without producing any apparent alteration in its condition.

The dog shows some remarkable symptoms. If the stomach contents are injected into this animal subcutaneously he presents symptoms of slight infection, manifested by restlessness, loss of appetite, etc. After twenty-four hours he recovers, and some days later an abscess forms at the point of infection.

After injection of my culture the dog shows the same disturbances, but no abscess forms. I have not injected the contents of the stomach into the abdomen of the dog, but in injecting 5 c. c. of my culture into the peritoneal cavity, general and uncertain morbid symptoms showed themselves. These last about two days. A dog weighing 10 kilos injected with 10 c. c. dies with symptoms of poisoning.

If the injection of culture in a dog results in no appreciable reaction, and if injection of the contents of the stomach produced only an abscess, and if again we make an injection stronger than the first and the dog reacts little, but does not die, I think these facts should be taken as signs of the commencement of immunization. Last year I increased the immunization of the dog to such a degree that the injection of its serum saved guinea pigs which had been injected with my culture, while the control animals died. At that time my labors were not sufficiently established, and I refer to the fact cited above only in passing. I propose to recur to it again.

The bacillus of which I speak tends to lose its virulence rapidly and at the same time to change its form, which is a species of degeneration. The virulent culture shows great numbers of bipolar bacilli, which transform themselves into uniform rods. In old cultures these rods became longer at the same time that their virulence greatly diminishes. When we pass these cultures through animals we restore the toxicity of the microbe, and if we continue these passages they again deteriorate.

In my former experiments and those of this year I verified the results as to the toxicity of the bacillus, as follows:

When a bouillon culture of some days growth is filtered and we inject the filtered liquid even in large quantities into a guinea pig the animal remains alive. When there have been errors in the experiment some microorganisms may pass through the filter and cause the death of the animal, but there is no toxic substance present. I forestalled this objection by passing the liquid through three Pukal filters at the same time that I made cultures of the filtered liquid and injected. The experiment had no value except when the cultures remained sterile. The result is that the toxic substance of the bacillus does not diffuse itself throughout the liquid but remains inherent to its own body.

Another important fact is the following:

When a virulent bouillon remains for three hours at a temperature of 65° the bacilli die. They may be injected even in large quantities with impunity.

This fact proves that the toxic substance of the bacillus destroys itself with relative ease.

From this exposition of the subject I conclude that *yellow fever is a disease, the toxic specific agent of which enters into the stomach and intestines, where it develops. It is only in exceptional cases that it invades other organs, and then only in small quantities.* In the stomach and the intestinal tube it forms a toxic substance, probably by dissolution of the body of the bacillus by the digestive fluids. The reabsorption of this poison causes grave alterations in the disease and eventually death. The guinea pig may be made to swallow large quantities of the stomach contents of yellow fever cadavers, and whether the stomach (gastric juice) be neutralized or not the animal does not react. This is true also of the cultures. When I had injured the œsophagus or the walls of the stomach, slightly, the animals died, but in these cases there was infection of the blood, for bacilli were found in it. I hope that the future will solve this question, as the question relative to cholera was solved by Nicati, Rietsch, and Koch himself.

It took me some time to differentiate my bacillus from that of the colon. When my bacillus is very virulent, it occurs in large numbers in the bipolar form. The bacillus coli behaves in a very different fashion. The colon bacillus is very motile; mine is probably immotile. The first (colon) grows in smooth plaques on gelatin; the other, in the form of pin heads. The bacillus coli develops, on potato, in abundance, with a

brownish color; mine grows moderately, and has a grayish color. Doubtless the bacillus coli exists also in the stomach, but its special seat is the lower part of the intestines, where it develops perfectly, and it never exists in the stomach in as great quantity as the one described. It is not as virulent and does not kill as speedily as mine. The bacillus which I have described, belongs, however, to the group of the bacilli of the colon and of typhus. It serves as a transition between these and the bacilli of hæmorrhagic septicæma, with which it has also some points of resemblance, and this conclusion is very satisfactory to me, for the clinical picture of yellow fever resembles very much that of diseases produced by the bacilli of this group.

CUBA.

Smallpox and yellow fever in Cuban seaports.

July 20: The United States consul at Cardenas reports that during the week ended July 17 there was in that city 1 death from yellow fever.

July 19: The United States consul at Cienfuegos reports that during the week ended July 18 there were in that city 5 deaths from yellow fever.

July 23: The United States consul at Matanzas reports that during the two weeks ended July 21 there were in that city 7 deaths from yellow fever.

July 23: The United States sanitary inspector at Habana reports that during the week ended July 22 there were in that city 48 deaths from yellow fever and 3 deaths from smallpox.

July 17: The United States consul at Santiago de Cuba reports that during the two weeks ended July 17 there were in that city 42 deaths from yellow fever.

Sanitary report from Habana.

HABANA, CUBA, *July 23, 1897.*

SIR: I have the honor to submit the following report for the week ended Thursday, July 22, 1897:

By the reports from the military hospitals yellow fever is decreasing both in number of cases and deaths from that disease. There is certainly no reason for either of these conditions, as the weather continues warm and the rainy season is at its height, with plenty of material on which the fever could feed.

Up to the last two weeks it was noticed that there were no cases occurring among the sailors of the Spanish navy, but lately five or six war vessels have gone to the navy yard, which is in close proximity to the Tallapiedra Wharf and closely adjoins a military hospital, where several cases have developed in the crews of said vessels. There are seven or eight war vessels now in the harbor and their complement must aggregate 1,500 men, many of whom, I learn, are not acclimated. This being true they will be doubly exposed to the danger of contracting the disease, being in close proximity to the worst infected wharves of the city.

But few cases are reported in the city and but one death outside of the military hospitals. Smallpox still exists to some extent, probably about 20 cases in the city, but few cases are reported in the military hospitals, and no deaths have occurred in those institutions in two weeks. The deaths from intestinal diseases have increased rapidly and have greatly augmented the deaths from all causes.